# Self-curing acrylic formulations containing PMMA/PCL composites: Properties and antibiotic release behavior

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Received 2 August 2001; revised 28 September 2001; accepted 22 October 2001

**Abstract:** Partially biodegradable acrylic composites containing poly(methyl methacrylate)–poly(ε-caprolactone) (PMMA/PCL) systems were prepared by mixing the corresponding PMMA/PCL beads (89:11, 86:14, 83:17, and 77:23 weight ratio) used as solid phase with methyl methacrylate (MMA) (liquid phase) in a solid/liquid ratio of 1.5:1. The physical and chemical microheterogeneity of these beads influenced significantly the curing parameters, because several aspects involved in the polymerization reaction are closely related to both morphology and size distribution of the particles. *In vitro* behavior was studied by immersion in simulated body fluid at pH = 7.4 and 37°C for more than 8 weeks and the composition was followed by $^1$H-nuclear magnetic resonance spectroscopy. Approximately 2% wt/wt weight loss was observed after a period of 8 weeks for the composites richest in PCL. Mechanical properties of the dry and wet specimens were evaluated by compressive and tensile tests. In all cases, the presence of PCL in the composites provided a significant decrease in both compressive strength and elastic modulus compared with plain PMMA. Tensile and compressive strength also decreased significantly after 2 weeks of immersion in simulated body fluid compared with dry specimens. The self-curing composites based on PMMA/PCL beads and loaded with 3% wt/wt vancomycin were evaluated as carriers for local release of antibiotics. The composite prepared with beads of PMMA/PCL ratio 86:14 was the most effective. It eluted 64% of the initial drug within the first 5 h, allowing progressive release of nearly the total amount of the initial drug (90%) in approximately 2 months. The results obtained suggest that the described composites can be suitable for antibiotic release in non-load bearing graft applications. © 2002 Wiley Periodicals, Inc. J Biomed Mater Res 61: 66–74, 2002

**Key words:** self-curing formulations; partially biodegradable composites; bone graft; poly(ε-caprolactone); vancomycin release

## INTRODUCTION

Synthetic biodegradable and biocompatible polymers such as poly(α-hydroxy acids), poly(β-hydroxyalkanoates), poly(dioxanone), poly(trimethylene carbonate), poly(ε-caprolactone) (PCL), polyanhydrides, polyorthoesters, and other materials have found a multitude of biomedical uses.[1,2] They have been extensively studied because of their important biomedical applications including controlled drug delivery systems, surgery, tissue engineering, and other biomedical fields.[3,4] In orthopedic applications, the development of bioresorbable polymers for use as degradable devices has been widely investigated in the last 30 years. Presently, numerous biodegradable devices, such as fracture and craniomaxillofacial fixation devices, interference screws, suture anchors, and meniscus repair, among others, are commercially available.[5] Another exciting application of these materials is their potential as drug delivery systems. Thus, the delivery of a bone morphogenic protein may be used to speed the healing process after a fracture,[6] or the delivery of antibiotics may help prevent osteomyelitis after surgery.[7]

The preparation of reinforced systems based on poly(L-lactic acid)[8,9] or based on poly(glycolic acid)[10] has been investigated to improve the mechanical strength of the systems during the biodegradation process. In addition, the design of drug delivery systems with appropriate mechanical properties has led to the development of partially biodegradable composites.[11,12] In that direction, Leenslag et al.[11] have proposed the preparation of composites based on polyurethane and polylactide reinforced with carbon fibers for the reconstruction of menisci, and poly(methyl methacrylate) (PMMA) has been used as a biostable and biocompatible component for orthopedic implants. Thus, a biodegradable phase is dispersed in a continuous biostable acrylic matrix, and its bio-

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Contract grant sponsor: CICYT; contract grant number: MAT99-1064-C02-01

degradation allows the ingrowth of osseous tissue inside the implanted devices during the repairing healing process.[12]

Most of the acrylic–bone grafts and cements widely used in orthopedic applications are made by *in situ* polymerization of MMA in the presence of a prepolymerized component, PMMA beads, to reduce polymerization temperature and volume shrinkage occurring during polymerization, while adjusting the viscosity and reaction kinetics.[13] The incorporation of beads containing PCL, a biodegradable polymer, seems to be an interesting way to get partially biodegradable composites.

PCL is a very well known biodegradable aliphatic polyester with interesting properties and applications in the biomedical field.[14,15] Because of its very slow degradation rate, it was proposed for a number of applications including absorbable devices and long-term drug delivery systems.[14,16–18] However, PCL copolymers or blends have lower overall crystallinity than the homopolymer, leading to a higher accessibility of ester linkages and an enhanced rate of hydrolysis.

In this article, the preparation of self-curing acrylic formulation containing PMMA/PCL composites, is described. Properties such as curing parameters, hydration behavior, morphology, and mechanical performance of these partially biodegradable systems are shown. Finally, the release profile of different vancomycin-loaded formulations is discussed.

## MATERIALS AND METHODS

### Materials

MMA 99% (Acros Organics) was used as received, benzoyl peroxide (BPO) (Fluka) was purified from fractional recrystallization from ethanol, mp = 104°C. 4-Dimethylaminobenzyl alcohol was synthesized by reduction of the corresponding benzaldehyde in our laboratory.[19]

### Preparation and characterization of acrylic-based formulations

The PMMA/PCL beads used in this work were obtained by suspension polymerization method.[20] Briefly, PCL ($M_n$ = 45,000) was dissolved in MMA in different proportions (i.e.: 10, 15, 20, and 30% PCL wt/monomer wt) under vigorous stirring. The initiator, BPO (1.5% wt/wt monomer) was then dissolved in the mixture, poured into a reactor containing a 2% poly(vinyl alcohol) solution as suspension agent, and stirred at 600 rpm. After a heating program, spherical beads containing different amounts of PCL (PMMA/PCL weight ratio: 89:11, 86:14, 83:17, and 77:23) were obtained.

The size distribution of the synthesized beads was determined by means of a video camera, Sony CCD-IRIS, coupled to an optical microscope (Nikon Eclipse E400), using polarized light and dark field. The data were statistically treated after the determination of the dimensions of 1000 particles randomly distributed in different images. Number-average diameter ($d_n$) was calculated according to the following expression:

$$d_n = \Sigma n_i d_i / \Sigma n_i$$

where $d_i$ is the mean diameter of each particle calculated from the average of $d_x$ and $d_y$.

PMMA-based composites were obtained by using MMA as liquid phase, BPO as initiator (1.5% wt/solid wt), 4-dimethylaminobenzyl alcohol (1% wt/liquid wt) as a low toxicity activator,[21] and PMMA/PCL beads with different PCL content, as solid phase. A solid/liquid ratio (s/l) of 1.5:1 was used. The reactive mixture was allowed to cure in the molds at 37°C for 1 h. No external pressure was applied at any time during the curing process.

Residual monomer content was determined by $^1$H-nuclear magnetic resonance (NMR) spectroscopy in a Varian Gemini spectrometer operating at 200 MHz. NMR spectra were obtained at room temperature from 5% wt/v $CDCl_3$ solutions. Specimens were stored in air for 7 days before the analysis.

The curing characteristics of PMMA and PCL-containing formulations, such as setting time and peak temperature, were evaluated using a Teflon mold maintained at 25°C according to ASTM F451 standard. Tensile experiments as well as compression test were conducted at room temperature on an Instron 4301 universal testing machine. The tensile tests were performed according to ISO 527-1 procedure, using a crosshead displacement rate of 1 mm/min at room temperature whereas the compression ones were performed by using 20 mm/min crosshead rate according to ASTM F451 standard. The deformation was calculated directly from the crosshead speed and the yield stress was determined in compression for each specimen at the maximum stress.[22] A minimum of five specimens from each batch were mechanically tested. One-way analysis of variance was performed for mechanical properties results at 0.05 level of significance ($p$ = 0.05). Significant differences of the mechanical properties of PMMA/PCL specimens with respect to PMMA cement and with respect to the value of previous period of immersion time were determined.

### *In vitro* behavior

To evaluate the *in vitro* behavior of the prepared formulations, composite samples were immersed in simulated body fluid (SBF) (pH = 7.4).[23] The composition of the immersed samples was determined by using $^1$H-NMR spectroscopy. Water uptake values were evaluated gravimetrically at different periods of time at 37°C. At appropriate times, the samples were removed, blotted quickly with absorbent paper to remove the water attached on its surface, and weighed. In all the experiments, a minimum of three samples were measured and averaged. The hydration de-

gree of the samples was calculated from the following relation:

$$\text{Hydration degree (\%)} = [(W_t - W_o)/W_o] \cdot 100$$

where $W_t$ is the weight of swollen specimen at time $t$ and $W_o$ is the initial mass of the specimen.

The morphology of dried samples and samples immersed in SBF was examined by using a scanning electron microscope, Hitachi FEG S-800.

### Preparation of drug-loaded samples and drug-release measurements

Vancomycin hydrochloride powder (Combinopharm) was selected as antibiotic with probed bactericidal effects and low allergic reactions. Antibiotic-loaded samples were prepared by mixing a predetermined amount of vancomycin powder with PMMA/PCL beads. The mixture was then incorporated into the composite formulation as solid phase as described above, the vancomycin concentration in the sample being 3.0% wt/wt. Rectangular-shaped samples (10 × 100 mm) and 1-mm thickness were prepared for elution experiments.

An *in vitro* elution method was used to determine the release behavior of loaded formulations. The samples were immersed in vials containing 15 mL of phosphate buffer (Titrisol, 0.026 mol/L $KH_2PO_4$, 0.041 mol/L $Na_2HPO_4$; Merck) (pH = 7) and incubated at 37°C without stirring. The dissolution medium was collected at different periods of time and analyzed. Fresh phosphate buffer (15 mL) was then added for the next period. The release measurements were determined by means of high-performance liquid chromatography, PerkinElmer LC-250 pump, a UV-Vis detector PerkinElmer LC-95, and a Waters μBoundapack C-18 column of 3.9 × 300 mm. The wavelength used was 215 nm. A methanol/aqueous solution of PIC-A (Waters) (60:40) was used as the mobile phase and flow rate of 1 mL/min. All samples were assayed in triplicate. The retention time of the vancomycin peak in samples relative to the standard was 2.95 ± 0.05 (mean ± SD, $n$ = 200). The calibration curve was made for the complete set of the measurements, displaying a correlation coefficient of 0.9957.

## RESULTS AND DISCUSSION

### Composition, morphology, and size distribution of PMMA/PCL beads

PMMA/PCL microparticles prepared by free radical polymerization of MMA/PCL solutions in water suspension are not a pure blend of PMMA and PCL polymers. During the polymerization of MMA, a graft copolymer of PCL onto PMMA chains is produced to some extent. In fact, the small fraction that remained insoluble in chloroform could be produced by the formation of PCL macroradicals in the presence of the initiator.[9,20] The segregation of PCL microdomains depends on the fraction of PCL in the reaction medium and the conversion ratio, and the formation of graft copolymers could stabilize the formed microdomains. Figure 1(a,b) shows scanning electron microscopy (SEM) pictures of these beads. The observed morphology patterns are quite complex, as a result of complexity of the suspension polymerization process and melting-crystallization of PCL microdomains.[20]

Particle size distribution as a function of composition is shown in Figure 2. For the experimental conditions used in this work, the number-average diameter of the particles increased with the PCL content. Beads of PMMA/PCL 100:0, 89:11, and 86:14 ($d_n$ = 14.35, 57.46, and 74.28 μm, respectively) exhibited a unimodal distribution whereas those having higher PCL contents, with compositions such as 83:17 and 77:23 ($d_n$ = 138.23 and 140.12 μm, respectively), displayed a multimodal profile, which could be related to the physical and chemical microheterogeneity of these

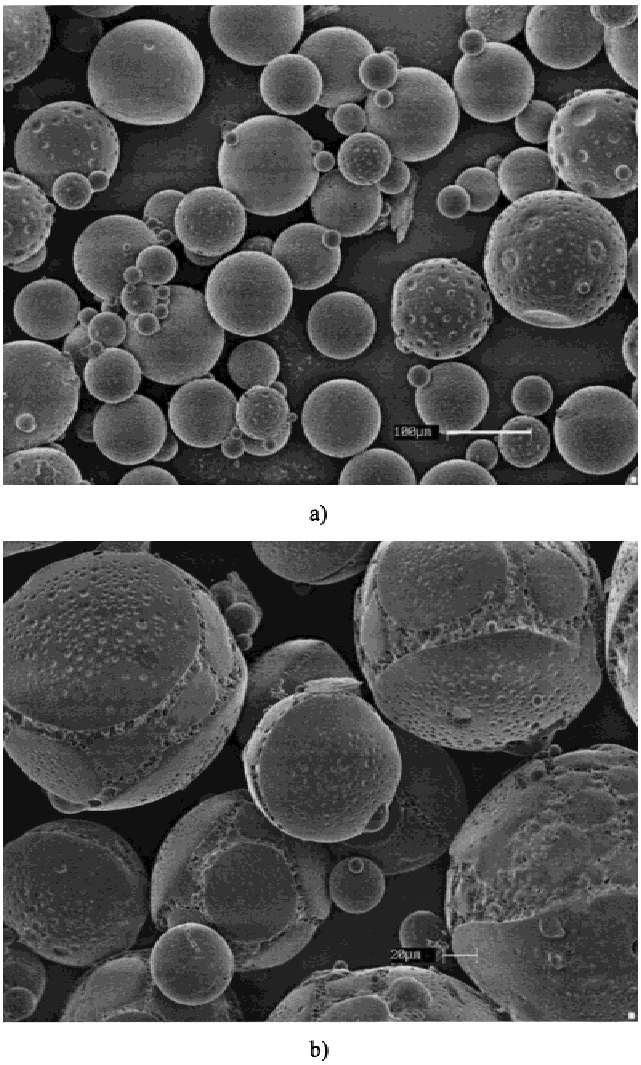

**Figure 1.** SEM pictures of PMMA/PCL beads: (a) 89:11, (b) 83:17.

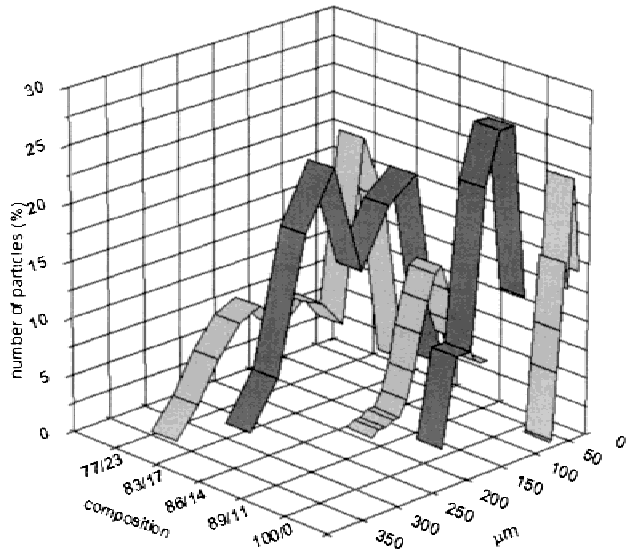


**Figure 2.** Size distribution profiles of the synthesized beads.

systems.[20] This fact is expected to influence significantly the curing parameters, because swelling and partial dissolution of the beads, viscosity evolution during the free radical polymerization, and heat dissipation among other aspects are closely related to both morphology and size distribution of the particles.[24]

## Curing of the composites

The temperature–time profiles of the cements prepared with PMMA/PCL beads of different compositions are shown in Figure 3. Values of peak temperature were under the standard limits in all formulations, a decrease being observed for the cements prepared with 14 and 23% PCL containing beads, probably because of the different size distribution of these beads as well as the content and distribution of PCL within them. Values of setting time were in the range of 7–9 min for the formulations containing 14 and 17% PCL beads, and approximately 13 min for that containing the highest amount of PCL. These beads were less soluble in the MMA. Samples containing more than 25% PCL were not used due to the high viscosity of the mixture.

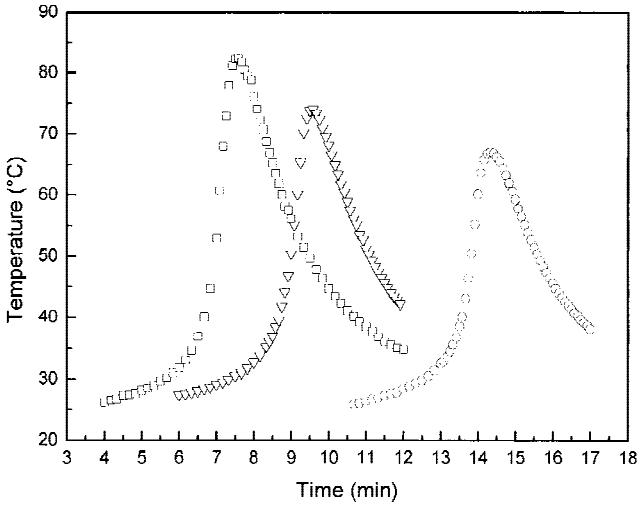


**Figure 3.** Evolution of temperature during the cure of samples with different PMMA/PCL ratios: (▽) 86:14, (□) 83:17, and (○) 77:23.

The degree of monomer conversion in PMMA formulations is well known to be limited by the vitrification phenomenon, cure temperature, and mold dimensions, leading to cured materials with a certain amount of unreacted monomer. Toxic effects against cells and tissues caused by the presence of a high concentration of monomer before and during the polymerization have been reported.[25] The residual monomer can also produce several effects in some mechanical properties.[26,27] The composites studied in this work presented residual monomer values in the range of 2–3% wt/wt independently of the PCL content, as determined by NMR spectroscopy. These values are in the range of those found in conventional PMMA cements[28] and indicate that the conversion of the polymerization reaction of MMA in the presence of different proportions of PCL reached values similar to those obtained in PMMA cements.

## *In vitro* behavior

Composites of different composition were immersed in SBF and the weight loss was determined by NMR spectroscopy. A small decrease of the fraction of PCL in the composite was obtained with time, as shown in Figure 4. The composites richest in PCL showed a weight loss close to 2% wt/wt, whereas for the composite prepared with the lowest content of PCL, the degradation was negligible. Pure PCL is known to degrade very slowly in an aqueous medium because of its semicrystallinity and hydrophobic structure which avoids fast water penetration.[29] Nevertheless, this fact could be attributed mainly to degradation of segregated microdomains of PCL produced by the incompatibility of PCL with the PMMA matrix,[20] which occurs by random hydrolytic chain scission of the ester linkages in the amorphous segments.

Figure 5 shows the hydration degree of PMMA and PMMA/PCL composites with time of immersion in SBF. These values were calculated according to the equation given in the experimental section, which did not take into account the weight loss of the sample. Water uptake values were in the range of 1.5–2%, that

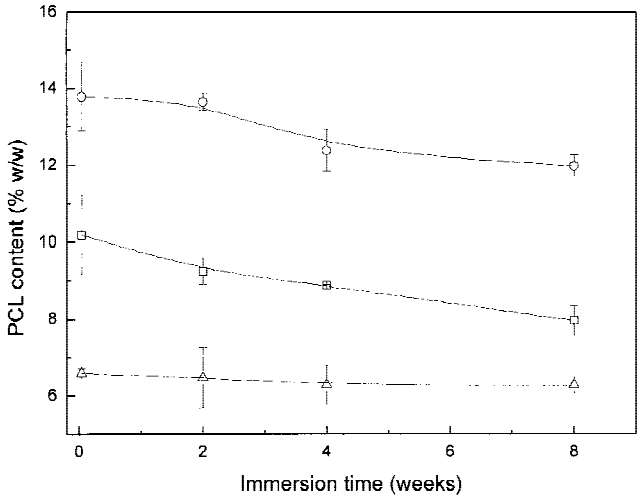


**Figure 4.** PCL content determined by NMR as a function of immersion time in SBF for samples containing different PMMA/PCL ratios: (△) 89:11, (□) 83:17, and (○) 77:23.

is, close to that of plain PMMA cement, remaining almost constant after 4 weeks, that was expected because of the hydrophobic character of the PCL chains. However, they reached values slightly superior if weight loss is considered.

The surface morphology of dry and wet acrylic composites was examined by using SEM and is shown in Figure 6. After immersion in SBF for 2 months, the surface morphology presented more defined microporous, interconnected channels and, to some extent, surface erosion.

### Variation of residual monomer content

A decrease of residual monomer content with immersion time in SBF was observed, the release being

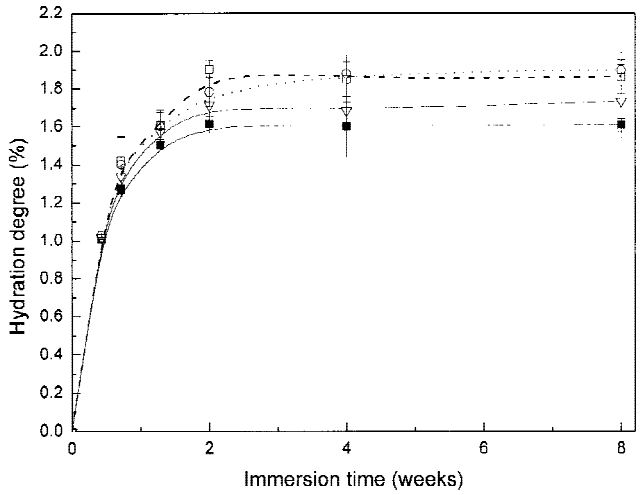


**Figure 5.** Hydration degree of samples immersed in SBF at 37°C. PMMA/PCL ratios: (■) 100:0, (▽) 86:□14, (□) 83:○17, and (○) 77:23.

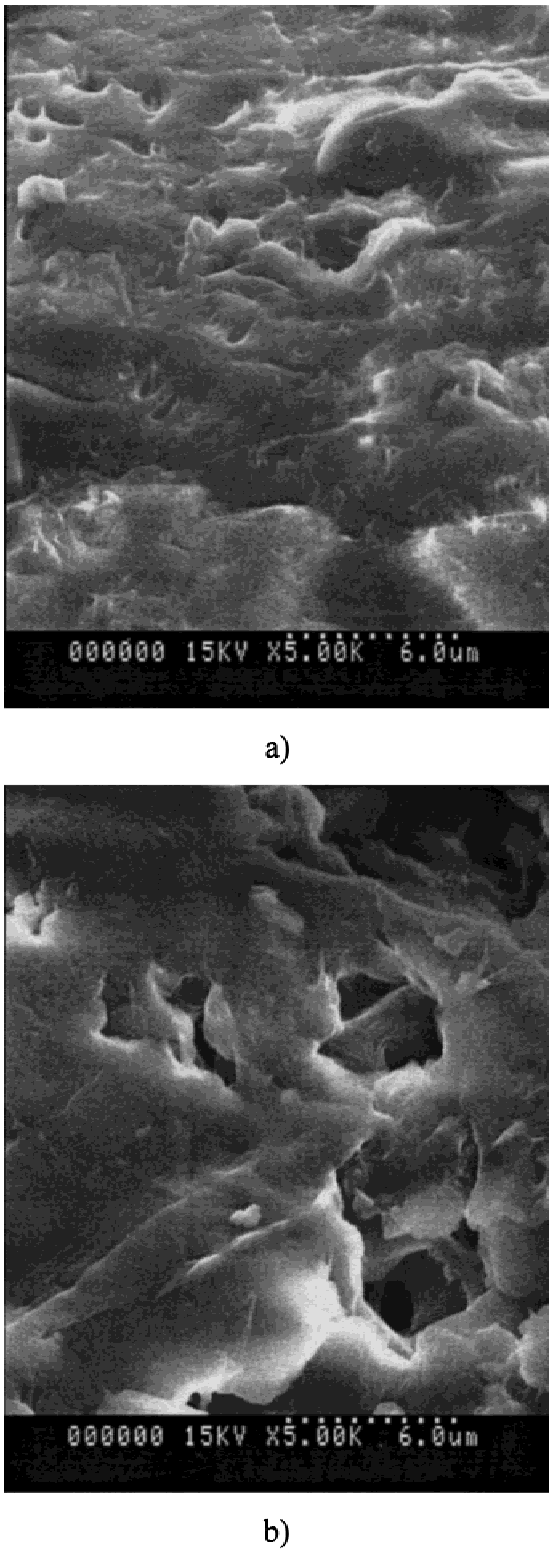


**Figure 6.** SEM micrographs of composite PMMA/PCL 83:17: (a) original sample, (b) after immersion in SBF for 2 months.

dependent on the composition of the solid phase (Fig. 7). The release of MMA decreased with time for the PMMA sample reaching values close to 1.5% in 8 weeks. This result is consistent with previous studies

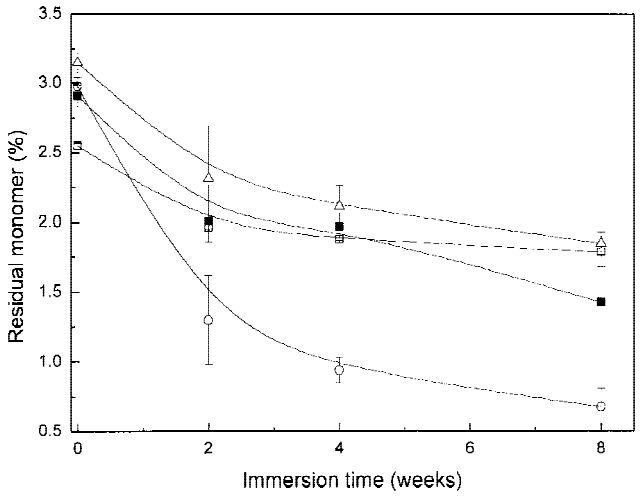


**Figure 7.** Residual monomer content of samples immersed in SBF determined by NMR. PMMA/PCL ratios: (■) 100:0, (△) 89:11, (□) 83:17, and (○) 77:23.

on PMMA acrylic bone cements. Brauer et al.[30] found that after 4.5 months in water without stirring, the monomer content is reduced to 1.4%. Other studies reported that the residual content of MMA in pellets of commercial bone cement formulations decreased with time of immersion in water up to levels close to 1.5% in 3 weeks' time.[31] As is known, in PMMA cement, the monomer is trapped in the bulk of the cement and release of the residual requires bulk diffusion to the surface. However, for the composites containing PCL, the majority of the residual MMA was released from the composite during the first 2 weeks and this effect was more evident with increasing PCL content in the cement, indicating that the presence of PMMA/PCL beads embedded into the acrylic matrix influenced the release of the residual MMA. This fact can be accounted for by the heterogeneity and the morphological characteristics of the composites prepared with PMMA/PCL beads, because the degradation process is scarce at this period of time.

## Mechanical properties

The results of the variation of the mechanical properties with time of immersion in SBF as assessed by tensile and compressive tests are summarized in Tables I and II.

Tensile strength and strain to break decreased significantly with PCL content for dry and wet specimens at any time of immersion, which can be attributed to the introduction of PCL, a semicrystalline polymer with poor mechanical properties.[32–34] The degree of crystallinity of the PCL incorporated in the beads of PMMA/PCL ratios of 86:14 and 83:17 has been found to be 0.35 and 0.46, respectively.[20] In addition, the low

**TABLE I**
**Tensile Test Results: Maximum Tensile Stress (Tensile Strength) ($\sigma_M$), Tensile Strain at Tensile Strength ($\varepsilon_M$), and Young's Modulus ($E_t$) at Different Immersion Times in SBF at 37°C**

| PMMA/PCL Composition | 0 Weeks | 2 Weeks | 4 Weeks |
|---|---|---|---|
| $\sigma_M$ (SD) (MPa) | | | |
| 100:0 | 49.4 (3.0) | 36.5 (2.4)* | 34.2 (2.5)* |
| 86:14 | 29.9 (2.3) | 20.3 (2.1)* | 18.8 (1.2) |
| 83:17 | 17.3 (0.8)† | 10.6 (1.6)* | 9.8 (2.6) |
| $\varepsilon_M$ (SD) (%) | | | |
| 100:0 | 7.4 (0.9) | 3.4 (0.5)* | 2.8 (0.2) |
| 86:14 | 4.6 (0.6) | 2.0 (0.1)* | 1.6 (1.2)*† |
| 83:17 | 1.3 (0.1)† | 1.1 (0.2)*† | 0.9 (0.2)† |
| $E_t$ (SD) (MPa) | | | |
| 100:0 | 1144 (56) | 1270 (109) | 1516 (73)* |
| 86:14 | 965 (22)† | 1278 (169)* | 1356 (61)† |
| 83:17 | 1187 (53) | 1288 (85) | 1308 (84)† |

*Significant differences compared with the value of previous period of immersion time in each row.
†Significant differences compared with PMMA in each column.

compatibility between both PCL and PMMA chains within the composite will contribute to the reduction of these parameters. After conditioning in SBF, a significant decrease of both tensile strength and strain to failure was observed in all specimens for a 2-week period with respect to the corresponding dry specimen. The reduction of strength in wet specimens can be mainly attributed to the plasticizing effect produced by the ingress of water molecules in the composite, which in addition is slightly higher for the cements containing PCL (Fig. 5). Young's modulus decreased significantly ($p$ = 0.00108) for the cement containing 14% PCL beads but no significant changes were observed for that containing 17% PCL beads compared with the dry PMMA sample. A reduction of Young's modulus with PCL content is consistent with previous experiments on the dynamic mechanical

**TABLE II**
**Compression Test Results: Yield Stress ($\sigma_y$) and Young's Modulus ($E_c$) at Different Immersion Times in SBF at 37°C**

| PMMA/PCL Composition | 0 Weeks | 2 Weeks | 4 Weeks |
|---|---|---|---|
| $\sigma_y$ (SD) (MPa) | | | |
| 100:0 | 112.8 (7.0) | 100.3 (5.3)* | 89.5 (6.2)* |
| 86:14 | 75.2 (7.4)† | 68.7 (3.8)*† | 69.2 (3.2)† |
| 83:17 | 55.9 (6.8)† | 57.4 (3.1)† | 47.1 (3.4)*† |
| $E_c$ (SD) (MPa) | | | |
| 100:0 | 1453 (66) | 1359 (99) | 1274 (81) |
| 86:14 | 1216 (91)† | 1103 (94)† | 1138 (76)† |
| 83:17 | 1115 (84)† | 1058 (41)† | 869 (60)*† |

*Significant differences with respect to the value of previous period of immersion time in each row.
†Significant differences with respect to PMMA cement in each column.

thermal analysis of these PMMA/PCL beads that showed a decrease in storage modulus measured at the beginning of the experiment with the content of PCL.[20] After storage in SBF, Young's modulus increased significantly ($p = 0.013$) after 2 weeks of immersion with respect to dry specimen for the cement containing 14% PCL beads but values of elastic modulus for wet specimens prepared with 17% PCL beads were not significantly different.

Accordingly, the presence of PCL in the composites provided a significant decrease in both compressive and tensile strength but a moderate decrease of the elastic modulus either in dry or wet specimens compared with PMMA. Values of compressive strength for specimens conditioned in SBF were significantly lower than those of the corresponding dry specimens. The cement prepared with beads of PMMA/PCL ratio 86:14 presented a significant ($p = 0.0023$) decrease in strength in 2 weeks' time whereas the cement prepared with beads containing 17% PCL showed a significant ($p = 0.013$) reduction of strength in a period of 4 weeks. Values of Young's modulus in compression did not significantly change with immersion and only a significant decrease ($p = 0.0029$) was observed for the cement containing 17% PCL beads after 4 weeks of immersion.

### Vancomycin-loaded composites

Current antibiotic delivery systems for orthopedic infection treatment use PMMA bone cement beads as drug release. The elution of antibiotic (gentamicin) from these beads is bimodal. Initially, a relatively fast release of 5% of the total amount of antibiotic occurs within the first 24 h and the release diminishes progressively to undetectable levels within a few weeks or months.[35] The use of PMMA beads impregnated with vancomycin in the treatment of chronic osteomyelitis were first introduced by Scott et al.[36] Later, vancomycin was incorporated in the acrylic bone cement formulations.[37] Partially biodegradable bone cements based on the crosslinking reaction between a prepolymer of poly(propylene fumarate) with MMA monomer impregnated with vancomycin have been developed by Gerhart et al.[38] Recently, new bioactive bone cements have been developed to be used as devices for drug delivery systems.[39,40]

Thus, the PMMA/PCL composites prepared in this work can offer an alternative to the current drug delivery systems which can be polymerized *in vivo* and also supply both structural support and partial biodegradation. Beads of PMMA/PCL ratios of 86:14 and 77:23 were chosen for these experiments. The composite with PMMA/PCL ratio 77:23 was prepared with an s/l ratio of 1.3:1 to get a good dispersion of the antibiotic and the beads. In these conditions, the formulation is fluid enough to be injected during at least the first 6–7 min, which allows an easy manipulation and application. Curing parameters of these composites were measured in the presence of vancomycin, giving rise to values of peak temperature close to 70°C in both cases. However, a value of setting time of 10 min was obtained for the composite prepared with the smallest beads, whereas a value of 14 min was measured for the another one, which can be attributed to the decrease in the s/l ratio of the latter formulation. Figure 8 shows the vancomycin release profiles for loaded PMMA/PCL composites along with that of loaded PMMA used as control. In all cases, the release of vancomycin was initially fast and then slowed down. For the PMMA cement, the majority of the vancomycin (23% of the incorporated amount) was released in the first 9 h (burst effect) and from then on, a slow release was observed, leaching the 29% of the total initial drug after 2 months. This fact indicates that the drug diffuses quickly from the superficial zones but more slowly from deeper zones.[41] The cement prepared with beads of PMMA/PCL ratio 86:14 exhibited a more significant burst effect than plain PMMA, eluting 64% of the initial drug within the first 5 h. However, this composite allows progressive release of nearly the total amount of the initial drug (90%) in approximately 2 months. A higher amount of liquid phase (s/l = 1.3:1) was used for the cement prepared with beads containing the highest amount of PCL (77:23) which means a higher setting time and a higher amount of PMMA matrix once the polymerization reaction has finished, in which the beads remain embedded. In this case, the cement displayed an intermediate response; 45% of the loaded drug was released from the cement at the initial stage of the drug release and the remainder released more slowly to

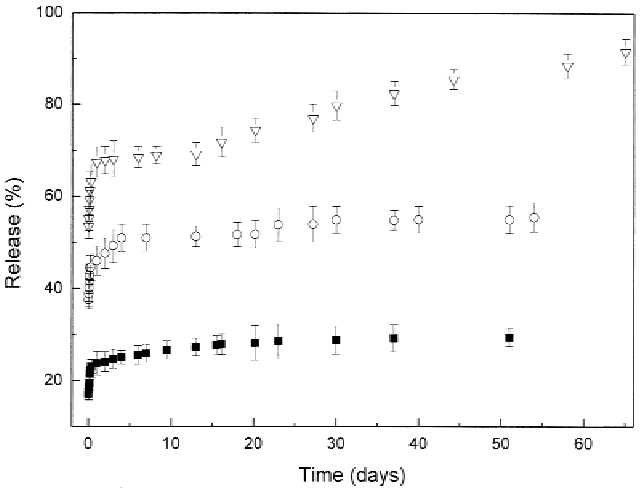


**Figure 8.** Vancomycin release profiles of samples with different PMMA/PCL ratios: (■) 100:0 (control), (▽) 86:14, (s/l = 1.5:1), and (○) 77:23 (s/l = 1.3:1).

reach a value of 55% of the initial amount in 40 days. The general trend of a high burst release followed by exponential decay has also been reported in the literature for other systems, e.g., the release of nonsteroidal anti-inflammatory drugs from PMMA bone cements.[42] The differences in the release of both composites can be attributed to differences in their formulations, as mentioned above. One interesting result is that, owing to the relatively low peak temperature reached in the curing process, the vancomycin does not suffer any chemical modification and guarantees the chemical stability of the antibiotic during the composite formulation, which has been tested by NMR spectroscopy of extracted vancomycin.

## CONCLUSIONS

PMMA/PCL composites are good candidates as partially biodegradable antibiotic-loaded systems with long-time controlled release, for non-load bearing surgical and clinical applications. The use of composite PMMA/PCL beads as a solid component of the acrylic formulation provides lower peak temperature and longer setting times than classical PMMA-based acrylic cements. The curing formulations proposed in this work are adequate to be easily injected, maintaining the chemical stability of the antibiotic molecules.

J. A. M. thanks CICYT for the fellowship awarded. G. A. A. is grateful to MEC of Spain, which provided a grant for his stay in Spain. The authors thank Laura Lechuga and Ana Calle of Instituto de Microelectrónica de Madrid CSIC, as well as Antonella Motta and Claudio Migliaresi of University of Trento, for SEM imaging.

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